REMARKS

This amendment is responsive to the June 10, 2010 Office Action. Applicant respectfully requests reconsideration of the application, withdrawal of all rejections, and allowance of the application in view of the remarks below. All references below to paragraphs in Applicant's specification refer to the specification as published: US 2008/0139670.

I. Amendments to the Claims

Claims 3, 6, 10, 12-24, 28, 29, 31, 32, and 40-46 are pending in the case of which claims 6, 10, 12-18, 22, 29, 40, and 41 are withdrawn. Claim 40 is cancelled and claims 28, 45, and 46 are amended. Specifically, the 3 claims are amended to incorporate the language of cancelled claim 40, language indicating the drug classes from which the drug molecule can be chosen. This amendment can be supported by Applicant's specification at, for example, paragraphs [0067] through [0080] and paragraph [0188].

Applicant reserves the right to file divisional or continuation applications directed to subject matter cancelled herein.

Applicant believes these amendments introduce no new material.

II. Miscellaneous Matters

Applicant thanks the Examiner for considering the March 25, 2010 Information Disclosure Statement.

III. Examiner Interview

Applicant thanks the Examiner for his time and consideration on September 7, 2010, in discussing the claims and the current rejections with Applicant's counsel, Paul J. Prendergast and Cara Crowley-Weber. During the interview, the Examiner clarified the parameters of his search and discussed several issues to facilitate counsel's understanding of the pending Office Action.

IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Examiner rejects claims 3, 19-21, 23-24, 28, 31-32, and 42-46 as lacking written description support in the specification for the claimed genus. Applicant respectfully disagrees and requests withdrawal of the rejection.

Evidence of possession of a claimed genus is provided by Applicant's specification and determined by the following factors: (a) the scope of the invention; (b) actual reduction to practice; (c) disclosure of drawings or structural chemical formulas; (d) relevant identifying

characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; (e) method of making the claimed compounds; (f) level of skill and knowledge in the art; and (g) predictability in the art.

While Applicant believes the claims as filed satisfy the written description requirement, in the interest of expediting prosecution, independent claims 28, 45, and 46 are amended herein to indicate the drug classes from which the drug molecule can be chosen: an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a Central Nervous System (CNS) drug, a sedative, and a steroid. Applicant believes this amendment addresses the Examiner's concerns. Specifically:

(a) The backbone structure of the conjugate is a thiodipeptide and the drug classes from which the drug molecule is chosen is provided within each claim. The scope of the claims is commensurate with the specification.

(b) and (e) Specific conjugate compounds were made by Applicant and are shown in Figures 1 and 6. Figures 2 through 4 provide structures and synthesis schemes for the conjugate compounds. The conjugate compounds contain drug analogs synthesized and tested including antibiotics, anticancer drugs, antihistamines, antihypertensives, antiinflammatories, antimalarials, antivirals, beta blockers, bronchodilators, cholesterol lowering agents, CNS drugs, sedatives, and steroids. See paragraphs [0067] through [0080], paragraphs [0139] through [0148]. Figure 7 provides data for more than 50 compounds tested for binding to and transport by PepT1. The activity of the conjugate for binding and transport was measured as the relevant endpoint for testing a carrier molecule.

(c) and (d) As mentioned above, structures and synthesis schemes for the conjugate compounds are provided in Figures 2, 3, and 4. Structures of conjugate compounds are shown in Figures 1 and 6. These structures represent a wide range of drug molecules. The structures correlate with the binding data and transport data shown in Figure 7, the compounds of which have the same thiodipeptide backbone. Thus, the claimed genus is supported by the description which provides a sufficient number of representative species to demonstrate possession.

(f) and (g) One skilled in the art could ascertain from the information provided in the Examples and Figures those compounds in possession by the inventor at the time the application was filed. Applicant clearly defines the R^1 and R^4 substituents on the thiodipeptide backbone (of

claims 28 and 46), provides classes of drug compounds for conjugating to the carrier (according to claims 28, 45, and 46), and tests the conjugate molecules in binding and transport assays. The predictability lies in the propensity of a conjugate molecule with a thiodipeptide backbone to bind PepT1 and be transported by the PepT1 pathway regardless of the drug attached to the carrier molecule through the R^4 linker, data for which is provided in the Examples and Figure 7.

As such, the Applicant's claims are sufficiently supported by the specification such that the written description requirement is more than satisfied.

V. Rejection of Claims Under 35 U.S.C. § 102

A. McElroy et al.

The Examiner rejects claims 3, 19-21, 23-24, 28, 31-32, and 42-46 as anticipated by McElroy et al. (Gly-(CSNH)-Phe resists hydrolysis by membrane dipeptidase. Biochemical Society Transactions. 1998 26(1), S31). In particular, the Examiner asserts the compound mentioned by McElroy et al. anticipates the genus of Applicant's claims. While Applicant respectfully disagrees, in the interest of expediting prosecution, the claims are amended to indicate the drug classes from which the drug molecule can be chosen. Applicant believes this amendment addresses the Examiner's concerns. Specifically:

Claim 28 is directed to a drug conjugate comprising a drug molecule attached to a thiodipeptide, where the drug molecule is covalently bonded to a functional group R^4 on the thiodipeptide. The claim requires that the drug molecule be an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid. Because the compound of McElroy et al. does not have a drug molecule, e.g. an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid attached to the C-terminal residue of the dipeptide, it cannot anticipate the conjugate compound of Applicant's claim 28. As such claim 28 is novel over McElroy et al.

Claims 3, 19-21, 23-24, 29, 31, 32, and 41-44 depend directly or indirectly from claim 28 and are therefore not anticipated for at least the same reason as discussed above with respect to claim 28.

Claim 45 is directed to a drug conjugate comprising a drug molecule covalently bonded to a thiodipeptide. The thiodipeptide has an N-terminal residue and a C-terminal residue; a drug

molecule is attached as a side chain of the C-terminal residue carboxylic acid residue. The claim requires that the drug molecule be an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid. Because the compound of McElroy et al. does not have a drug molecule, e.g. an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid attached to the C-terminal residue of the dipeptide, it cannot anticipate the conjugate compound of Applicant's claim 45. Thus, claim 45 is novel over McElroy et al.

Claim 46 is directed to a drug conjugate molecule as the product of the reaction of a functional group of a thiodipeptide with a drug molecule. A C-terminal functional group reacts with the drug molecule to covalently attach the drug molecule to the thiodipeptide. The claim requires that the drug molecule be an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid. Because the compound of McElroy et al. does not have a drug molecule, e.g. an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid attached to the C-terminal residue of the dipeptide, it cannot anticipate the conjugate compound of Applicant's claim 46. As such, claim 46 is novel over McElroy et al.

Further, McElroy et al. were testing mammalian membrane dipeptidase to determine whether the enzyme had broader substrate specificity, i.e. whether the enzyme was capable of hydrolyzing a thionopeptide bond. McElroy et al. neither teach nor suggest thiodipeptides covalently linked to a drug through a linker on the C-terminal residue of the dipeptide. In contrast, it was Applicant who determined that a drug conjugated to the chiral carbon of the C-terminal residue on the thiodipeptide actively bound to PepT1 and translocated by PepT1. This finding is contrary to the teachings in the art which demonstrate the importance of designing potential substrates of PepT1 to avoid steric hindrance from side chains attached to the C-terminal carbon.

There are no examples of thiodipeptide drug conjugates in the prior art, and as such, no examples of such conjugates used to enhance bioavailability in general (and via PepT1 in

particular). Contrary to the expectations in the art, Applicant demonstrated successful transport for a wide range of thiodipeptide drug conjugates.

As such, McElroy et al. alone or in combination with another publication does not obviate Applicant's invention.

B. Brillon et al.

The Examiner rejects claim 45 as anticipated by Brillon et al. (WO 91/01976). In particular, the Examiner asserts that because claim 45 does not recite a formula, the Ph-OH group mentioned by Brillon et al. is consistent with the compounds shown in Applicant's Figure 1, thus meeting the claim limitations of claim 45. Applicant respectfully disagrees.

In order to anticipate, Brillon et al. must show a thiodipeptide conjugated to a drug molecule attached as a side chain of the C-terminal residue carboxylic acid residue. 4-thiothymopentin is not a thiodipeptide, and Brillon et al. do not disclose a drug molecule covalently bound to a thiodipeptide through a C-terminal carboxylic acid linker. As such, Brillon et al. do not anticipate Applicant's claim 45.

However, in the interest of expediting prosecution, claim 45 is amended to require that the drug molecule is an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid. Because the compound of Brillon et al. does not have a drug molecule, e.g. an antibiotic, an anticancer drug, an antihistamine, an antihypertensive, an anti-inflammatory, an antimalarial, an antiviral, a beta blocker, a bronchodilator, a cholesterol lowering agent, a CNS drug, a sedative, or a steroid attached to the C-terminal residue of the dipeptide, it cannot anticipate the conjugate compound of Applicant's claim 45. As such, claim 45 is novel over Brillon et al.

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For the reasons set forth above, Applicant respectfully submits the claims as filed are allowable over the art of record and reconsideration and issuance of a notice of allowance are respectfully requested. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefor to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to deposit account No. 19-5117.

Respectfully submitted,

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